```
FILE 'HOME' ENTERED AT 15:27:57 ON 24 SEP 2008

=>
=> index bioscience
FILE 'DRUGMONOG' ACCESS NOT AUTHORIZED
COST IN U.S. DOLLARS                                SINCE FILE      TOTAL
                                                         ENTRY    SESSION
FULL ESTIMATED COST                                       0.21       0.21

INDEX 'ADISCTI, ADISINSIGHT, ADISNEWS, AGRICOLA, ANABSTR, ANTE, AQUALINE,
       AQUASCI, BIOENG, BIOSIS, BIOTECHABS, BIOTECHDS, BIOTECHNO, CABA, CAPLUS,
       CEABA-VTB, CIN, CONFSCI, CROPB, CROPU, DDFB, DDFU, DGENE, DISSABS, DRUGB,
       DRUGMONOG2, DRUGU, EMBAL, EMBASE, ...' ENTERED AT 15:28:11 ON 24 SEP 2008

69 FILES IN THE FILE LIST IN STNINDEX

Enter SET DETAIL ON to see search term postings or to view
search error messages that display as 0* with SET DETAIL OFF.

=> s (protease# or proteinase# or peptidase# (s) (metallocen## or ferrocene or
cobaltocene or chromocene or ruthenocene or nickelocene or titanocene)
UNMATCHED LEFT PARENTHESIS '(PROTEASE#'
The number of right parentheses in a query must be equal to the
number of left parentheses.

=> s (protease# or proteinase# or peptidase#) (s) (metallocen## or ferrocene or
cobaltocene or chromocene or ruthenocene or nickelocene or titanocene)
          1   FILE ANABSTR
          1   FILE BIOENG
          2   FILE BIOSIS
          8   FILE CAPLUS
          2   FILE DDFU
          2   FILE DGENE
          1   FILE DISSABS
          3   FILE DRUGU
  27 FILES SEARCHED...
          1   FILE EMBAL
          1   FILE EMBASE
          7   FILE IFIPAT
          2   FILE LIFESCI
          2   FILE MEDLINE
          1   FILE PASCAL
          5   FILE SCISEARCH
          1   FILE TOXCENTER
         16   FILE USPATFULL
          3   FILE USPAT2
  65 FILES SEARCHED...
          2   FILE WPIDS
          2   FILE WPINDEX

  20 FILES HAVE ONE OR MORE ANSWERS,   69 FILES SEARCHED IN STNINDEX

L1   QUE (PROTEASE# OR PROTEINASE# OR PEPTIDASE#) (S) (METALLOCEN## OR FERROCEN
         E OR COBALTOCENE OR CHROMOCENE OR RUTHENOCENE OR NICKELOCENE OR TITANO
         CENE)

=> s L1 and substrat##
          3   FILE CAPLUS
          2   FILE DGENE
          1   FILE DISSABS
          1   FILE DRUGU
```

```
         2   FILE IFIPAT
  37 FILES SEARCHED...
         1   FILE SCISEARCH
         5   FILE USPATFULL
         1   FILE WPIDS
         1   FILE WPINDEX

   9 FILES HAVE ONE OR MORE ANSWERS,   69 FILES SEARCHED IN STNINDEX

L2   QUE L1 AND SUBSTRAT##

=> d rank
F1           5   USPATFULL
F2           3   CAPLUS
F3           2   DGENE
F4           2   IFIPAT
F5           1   DISSABS
F6           1   DRUGU
F7           1   SCISEARCH
F8           1   WPIDS
F9           1   WPINDEX


=> fil f1, f2, f4-f9
COST IN U.S. DOLLARS                          SINCE FILE      TOTAL
                                                   ENTRY    SESSION
FULL ESTIMATED COST                                 4.55       4.76

FILE 'USPATFULL' ENTERED AT 15:32:11 ON 24 SEP 2008
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FILE 'WPINDEX' ACCESS NOT AUTHORIZED

=> s L2
L3          14 L2

=> dup rem L3
PROCESSING COMPLETED FOR L3
L4           13 DUP REM L3 (1 DUPLICATE REMOVED)

=> s L4 and py<2004
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L5 4 L4 AND PY<2004

=> d L5 ibib abs 1-4

L5 ANSWER 1 OF 4 USPATFULL on STN
ACCESSION NUMBER: 95:31790 USPATFULL <<LOGINID::20080924>>
TITLE: Immobilization of biologically active protein on a support with a 7-18 carbon spacer and a bifunctional phospholipid
INVENTOR(S): Kallury, Krishna M. R., Scarborough, Canada
Thompson, Michael, Mississauga, Canada
Lee, William E., Medicine Hat, Canada
PATENT ASSIGNEE(S): Her Majesty the Queen in right of Canada, as represented by the Minister of National Defence, Ottawa, Canada (non-U.S. government)

	NUMBER	KIND	DATE	
PATENT INFORMATION:	US 5405766		19950411	<--
APPLICATION INFO.:	US 1993-36867		19930325	(8)

	NUMBER	DATE
PRIORITY INFORMATION:	CA 1992-2064683	19920326

DOCUMENT TYPE: Utility
FILE SEGMENT: Granted
PRIMARY EXAMINER: Naff, David M.
LEGAL REPRESENTATIVE: Szereszewski, Juliusz
NUMBER OF CLAIMS: 20
EXEMPLARY CLAIM: 1
NUMBER OF DRAWINGS: 4 Drawing Figure(s); 4 Drawing Page(s)
LINE COUNT: 1200
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
AB Enzymes and certain other bioactive substances are immobilized on solid substrates which have sufficient functional groups such as hydroxyl or carboxyl. The bioactive substances are linked to the substrates through spacer compounds having a long open alkyl chain with 7-18 carbon atoms and also through phospholipid intermediates. The spacer compound is chemically linked to the substrate. The phospholipid is covalently linked to the spacer compound. Immobilized bioactive substances of the invention exhibit a marked increase in activity and stability. In a preferred embodiment, immobilized enzymes having a high degree of resistance to thermal inactivation are prepared.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

L5 ANSWER 2 OF 4 CAPLUS COPYRIGHT 2008 ACS on STN
ACCESSION NUMBER: 1981:79255 CAPLUS <<LOGINID::20080924>>
DOCUMENT NUMBER: 94:79255
ORIGINAL REFERENCE NO.: 94:12855a,12858a
TITLE: High acylation rates and enantioselectivity with cyclodextrin complexes of rigid substrates
AUTHOR(S): Trainor, George L.; Breslow, Ronald
CORPORATE SOURCE: Dep. Chem., Columbia Univ., New York, NY, 10027, USA
SOURCE: Journal of the American Chemical Society (1981), 103(1), 154-8
CODEN: JACSAT; ISSN: 0002-7863
DOCUMENT TYPE: Journal
LANGUAGE: English
AB Previous work has shown that the acylation of β-cyclodextrin by

p-nitrophenyl 3-trans-ferrocenylpropenoate is an excellent model for the 1st step in the serine protease-catalyzed hydrolysis of esters. Saturation kinetics were observed and rate accelerations on the order of 106 were attained. It is reported herein that improvement in the rate acceleration can be realized by freezing out residual rotational degrees of freedom in the acylation transition state. Partial immobilization of the acrylate side chain has been accomplished by bridging to the ferrocene nucleus, resulting in a nearly 10-fold increase in the rate acceleration. Furthermore, a high enantioselectivity in the acylation of β-cyclodextrin by this bridged substrate has been observed with a 20-fold rate difference for the 2 enantiomers. The absence of a differential solvent 2H isotope effect is offered as evidence that the enantioselectivity is not due to differential H-bonding in the transition state (general-acid catalysis). The determination of the absolute configuration of the fast enantiomer together with the known configuration of β-cyclodextrin has allowed the postulation of a geometric basis for the observed enantioselectivity.

L5 ANSWER 3 OF 4 DISSABS COPYRIGHT (C) 2008 ProQuest Information and Learning Company; All Rights Reserved on STN

ACCESSION NUMBER: 87:27586 DISSABS Order Number: AAR8803532

TITLE: CLEAVAGE OF STRUCTURALLY DISTINCT PROCOLLAGENS BY TYPE I/II PROCOLLAGEN N-PROTEINASE AND IRON-CONTAINING METALLOCENES AS ACTIVE SITE-DIRECTED INHIBITORS OF N-PROTEINASE

AUTHOR: DOMBROWSKI, KENNETH EDWARD [PH.D.]; PROCKOP, DARWIN J. [advisor]

CORPORATE SOURCE: RUTGERS THE STATE UNIVERSITY OF NEW JERSEY - NEW BRUNSWICK (0190)

SOURCE: Dissertation Abstracts International, (1987) Vol. 49, No. 1B, p. 96. Order No.: AAR8803532. 184 pages.

DOCUMENT TYPE: Dissertation

FILE SEGMENT: DAI

LANGUAGE: English

ENTRY DATE: Entered STN: 19921118
Last Updated on STN: 19921118

AB Type I/II procollagen N-proteinase is the enzyme that cleaves the N-propeptides from type I and type II procollagen, but not from type III procollagen. Here, the kinetic constants for the cleavage of several types of procollagen by chick type I/II N-proteinase were compared with the conformations of the cleavage sites as predicted from the primary structures.

The K$\sb{\rm m}$ values were essentially the same (0.2 μM) for chick type I procollagen, human type I procollagen, and chick type II procollagen. However, the V$\sb{\rm max}$ values differed over a 14-fold range. Calculations of the conformations of the cleavage sites indicated that the bonds cleaved in the three procollagens were all in an α-helical conformation. Chick type II procollagen, which had the highest V$\sb{\rm max}$ value, had the largest α-helical domain. In contrast, type III procollagen had a random coil conformation in the same region. The absence of an α-helical conformation probably explains the resistance of type III procollagen to cleavage by type I/II N-proteinase.

Structural alterations of the procollagen molecule were studied for their effects on type I/II N-proteinase processing. An increase in post-translational modification of the substrate did not affect cleavage of the N-propeptides. A proα1(I) homotrimer of human procollagen was cleaved by the enzyme at the same rate as normal heterotrimeric human type I procollagen. Incorporation of shortened proα chains into procollagen abolished the native conformation of

the substrate, and the protein was resistant to cleavage by N-proteinase.

Derivatives of ferrocene (Fc) were examined as active site-directed inhibitors of type I/II N-proteinase. The compounds were shown to be reversible, competitive and specific inhibitors of the enzyme. A carbonyl moiety α to the cyclopentadienyl ring of Fc was necessary for maximal inhibition, and selective modification increased the inhibitory effects. The active inhibitory species apparently contained iron in the +3 valence state since two ferrocenium (Fc$\sp{+}$) derivatives were very effective inhibitors: Fc$\sp{+}$COOH PF$\sb6$- (K$\sb{\rm i}$ $< 50 μM) and Fc$\sp{+}$FeCl$\sb4$- (K$\sb{\rm i}$ = 4 μM), and reduction of Fc derivatives with ascorbic acid abolished the inhibitory activity of the compounds. Fc derivatives also stabilized the enzyme to heat denaturation whereas Fc$\sp{+}$ derivatives did not.

L5 ANSWER 4 OF 4 DRUGU COPYRIGHT 2008 THOMSON REUTERS on STN
ACCESSION NUMBER: 1985-31020 DRUGU B <<LOGINID::20080924>>
TITLE: Metallocene Inhibition of Type I Procollagen N-Proteinase.
AUTHOR: Dombrowski K E; Prockop D J; Sheats J E
LOCATION: Piscataway, Lawrenceville, New Jersey, United States
SOURCE: Abstr.Pap.Am.Chem.Soc. (188 Meet., BIOL 72, 1984)
CODEN: ACSRAL ISSN: 0065-7727
AVAIL. OF DOC.: Department of Biochemistry, UMDNJ-Rutgers Medical School, Piscataway, NJ 08854, U.S.A.
LANGUAGE: English
DOCUMENT TYPE: Journal
FIELD AVAIL.: AB; LA; CT; MPC
FILE SEGMENT: Literature
AN 1985-31020 DRUGU B <<LOGINID::20080924>>
AB A series of derivatives of ferrocene (Fc) (I) and cobaltocene (II) were studied as inhibitors of type I procollagen N-proteinase, the enzyme responsible for cleaving the amino-terminal propeptide from type I procollagen.
ABEX In an assay using 14C-procollagen as substrate the mono- and dicarboxylic acid derivatives of (I) and (II) inhibited the enzyme with a Ki in the range 300-400 uM, FcCH2CH2COOH (III), (Ki 3000 uM); FcCH=CHCOOH (IV), (Ki 500-1000 uM) and FcC(O)CH2CH2COOH (V), (Ki 10-50 uM). The monocarboxylic acid derivative of (I) did not inhibit either mammalian nor bacterial collagenases nor thermolysin at concentrations less than 4 mM. Effects due to ferric ions were ruled out since this ion did not inhibit N-proteinase at concentrations less than 500 uM.

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